

glycosaminoglycan-binding sites

(bases 1 to 4342)

in osteoarthritic cartilage

REMARK

REFERENCE

**AUTHORS** TITLE

GeneRIF: Autocatalytic cleavage reveals multiple

Malfait, A.M., Liu, R.Q., Ijiri, K., Komiya, S. and Tortorella, M.D.

Inhibition of ADAM-TS4 and ADAM-TS5 prevents aggrecan degradation

```
J. Biol. Chem. 277 (25), 22201-22208 (2002)
  JOURNAL
   PUBMED
            11956193
            GeneRIF: Inhibition of ADAM-TS4 and ADAM-TS5 prevents aggrecan
  REMARK
            degradation in osteoarthritic cartilage.
REFERENCE
               (bases 1 to 4342)
            Westling, J., Fosang, A.J., Last, K., Thompson, V.P., Tomkinson, K.N.,
  AUTHORS
            Hebert, T., McDonagh, T., Collins-Racie, L.A., LaVallie, E.R.,
            Morris, E.A. and Sandy, J.D.
            ADAMTS4 cleaves at the aggrecanase site (Glu373-Ala374) and
  TITLE
            secondarily at the matrix metalloproteinase site (Asn341-Phe342) in
            the aggrecan interglobular domain
            J. Biol. Chem. 277 (18), 16059-16066 (2002)
  JOURNAL
   PUBMED
            11854269
  REMARK
            GeneRIF: has a specific cleavage site at the matrix
            metalloproteinase site in its interglobular domain
            6 (bases 1 to 4342)
REFERENCE
            Gao, G., Westling, J., Thompson, V.P., Howell, T.D., Gottschall, P.E.
  AUTHORS
            and Sandy, J.D.
            Activation of the proteolytic activity of ADAMTS4 (aggrecanase-1)
  TITLE
            by C-terminal truncation
            J. Biol. Chem. 277 (13), 11034-11041 (2002)
  JOURNAL
   PUBMED
            11796708
            GeneRIF: activation of proteolytic activity by C-terminal
  REMARK
            truncation
REFERENCE
               (bases 1 to 4342)
  AUTHORS
            Yamanishi, Y., Boyle, D.L., Clark, M., Maki, R.A., Tortorella, M.D.,
            Arner, E.C. and Firestein, G.S.
            Expression and regulation of aggrecanase in arthritis: the role of
  TITLE
            TGF-beta
            J. Immunol. 168 (3), 1405-1412 (2002)
  JOURNAL
            11801682
   PUBMED
            GeneRIF: Aggrecanase-1 is expressed by fibroblast-like synoviocytes
  REMARK
            from rheumatoid arthritis and osteoarthritis patients and is
            induced by cytokines, especially TGF-beta.
               (bases 1 to 4342)
REFERENCE
            Hirohata, S.
 AUTHORS
            ADAMTS family--new extracellular matrix degrading enzyme
  TITLE
            Seikagaku 73 (11), 1333-1337 (2001)
  JOURNAL
            11831030
   PUBMED
            GeneRIF: extracellular matrix degrading enzyme
  REMARK
REFERENCE
               (bases 1 to 4342)
            Nakamura, H., Fujii, Y., Inoki, I., Sugimoto, K., Tanzawa, K.,
 AUTHORS
            Matsuki, H., Miura, R., Yamaguchi, Y. and Okada, Y.
            Brevican is degraded by matrix metalloproteinases and aggrecanase-1
  TITLE
            (ADAMTS4) at different sites
  JOURNAL
            J. Biol. Chem. 275 (49), 38885-38890 (2000)
            10986281
  PUBMED
REFERENCE
            10 (bases 1 to 4342)
            Tortorella, M., Pratta, M., Liu, R.Q., Abbaszade, I., Ross, H., Burn, T.
 AUTHORS
            and Arner, E.
            The thrombospondin motif of aggrecanase-1 (ADAMTS-4) is critical
  TITLE
            for aggrecan substrate recognition and cleavage
            J. Biol. Chem. 275 (33), 25791-25797 (2000)
  JOURNAL
            10827174
   PUBMED
REFERENCE
            11 (bases 1 to 4342)
            Matthews, R.T., Gary, S.C., Zerillo, C., Pratta, M., Solomon, K.,
 AUTHORS
            Arner, E.C. and Hockfield, S.
            Brain-enriched hyaluronan binding (BEHAB)/brevican cleavage in a
  TITLE
            glioma cell line is mediated by a disintegrin and metalloproteinase
            with thrombospondin motifs (ADAMTS) family member
```

```
J. Biol. Chem. 275 (30), 22695-22703 (2000)
  JOURNAL
   PUBMED
            10801887
REFERENCE
            12 (bases 1 to 4342)
            Tortorella, M.D., Pratta, M., Liu, R.Q., Austin, J., Ross, O.H.,
 AUTHORS
            Abbaszade, I., Burn, T. and Arner, E.
  TITLE
            Sites of aggrecan cleavage by recombinant human aggrecanase-1
            (ADAMTS-4)
  JOURNAL
            J. Biol. Chem. 275 (24), 18566-18573 (2000)
   PUBMED
            10751421
REFERENCE
            13 (bases 1 to 4342)
            Hurskainen, T.L., Hirohata, S., Seldin, M.F. and Apte, S.S.
  AUTHORS
            ADAM-TS5, ADAM-TS6, and ADAM-TS7, novel members of a new family of
  TITLE
            zinc metalloproteases. General features and genomic distribution of
            the ADAM-TS family
            J. Biol. Chem. 274 (36), 25555-25563 (1999)
  JOURNAL
   PUBMED
            10464288
REFERENCE
            14 (bases 1 to 4342)
            Abbaszade, I., Liu, R.Q., Yang, F., Rosenfeld, S.A., Ross, O.H.,
 AUTHORS
            Link, J.R., Ellis, D.M., Tortorella, M.D., Pratta, M.A., Hollis, J.M.,
            Wynn, R., Duke, J.L., George, H.J., Hillman, M.C. Jr., Murphy, K.,
            Wiswall, B.H., Copeland, R.A., Decicco, C.P., Bruckner, R., Nagase, H.,
            Itoh, Y., Newton, R.C., Magolda, R.L., Trzaskos, J.M., Burn, T.C. et al.
  TITLE
            Cloning and characterization of ADAMTS11, an aggrecanase from the
            ADAMTS family
            J. Biol. Chem. 274 (33), 23443-23450 (1999)
  JOURNAL
   PUBMED
            10438522
REFERENCE
            15 (bases 1 to 4342)
            Tortorella, M.D., Burn, T.C., Pratta, M.A., Abbaszade, I., Hollis, J.M.,
 AUTHORS
            Liu, R., Rosenfeld, S.A., Copeland, R.A., Decicco, C.P., Wynn, R.,
            Rockwell, A., Yang, F., Duke, J.L., Solomon, K., George, H.,
            Bruckner, R., Nagase, H., Itoh, Y., Ellis, D.M., Ross, H., Wiswall, B.H.,
            Murphy, K., Hillman, M.C. Jr., Hollis, G.F., Arner, E.C. et al.
            Purification and cloning of aggrecanase-1: a member of the ADAMTS
  TITLE
            family of proteins
  JOURNAL
            Science 284 (5420), 1664-1666 (1999)
   PUBMED
            10356395
            16 (bases 1 to 4342)
REFERENCE
 AUTHORS
            Tang, B.L. and Hong, W.
 TITLE
            ADAMTS: a novel family of proteases with an ADAM protease domain
            and thrombospondin 1 repeats
  JOURNAL
            FEBS Lett. 445 (2-3), 223-225 (1999)
   PUBMED
            10094461
COMMENT
            REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AL603427.1, AB014588.1,
            AF148213.1 and AY358886.1.
            On Jan 26, 2004 this sequence version replaced gi:11497610.
            Summary: This gene encodes a disintegrin and metalloproteinase with
```

Summary: This gene encodes a disintegrin and metalloproteinase with thrombospondin motifs-4, which is a member of the ADAMTS protein family. Members of the family share several distinct protein modules, including a propeptide region, a metalloproteinase domain, a disintegrin-like domain, and a thrombospondin type 1 (TS) motif. Individual members of this family differ in the number of C-terminal TS motifs, and some have unique C-terminal domains. The enzyme encoded by this gene lacks a C-terminal TS motif. It is responsible for the degradation of aggrecan, a major proteoglycan of cartilage, and brevican, a brain-specific extracellular matrix protein. The cleavage of aggrecan and brevican suggests key roles of this enzyme in arthritic disease and in the central nervous system, potentially, in the progression of glioma.

```
COMPLETENESS: complete on the 3' end.
FEATURES
                     Location/Qualifiers
                     1..4342
    source
                     /organism="Homo sapiens"
                     /mol type="mRNA"
                     /db xref="taxon:9606"
                     /chromosome="1"
                     /map="1q21-q23"
                     1..4342
     gene
                     /gene="ADAMTS4"
                     /note="synonyms: ADMP-1, ADAMTS-2, ADAMTS-4, KIAA0688"
                     /db xref="GeneID:9507"
                     /db xref="LocusID:9507"
                     /db_xref="MIM: 603876"
                     428..2941
     CDS
                     /gene="ADAMTS4"
                     /note="a disintegrin-like and metalloprotease (reprolysin
                     type) with thrombospondin type 1 motif, 4; aggrecan 1;
                     aggrecanase-1;
                     go_component: extracellular matrix [goid 0005578]
                     [evidence IEA];
                     go function: metallopeptidase activity [goid 0008237]
                     [evidence E] [pmid 10356395];
                     go function: peptidase activity [goid 0008233] [evidence
                     E];
                     go function: zinc ion binding [goid 0008270] [evidence
                     IEA];
                     go function: metalloendopeptidase activity [goid 0004222]
                     [evidence IEA];
                     go process: proteolysis and peptidolysis [goid 0006508]
                     [evidence TAS] [pmid 10751421];
                     go_process: skeletal development [goid 0001501] [evidence
                     TAS] [pmid 10356395]"
                     /codon start=1
                     /product="a disintegrin and metalloproteinase with
                     thrombospondin motifs-4 precursor"
                     /protein id="NP 005090.2"
                     /db xref="GI:41327756"
                     /db_xref="GeneID:9507"
                     /db_xref="LocusID:9507"
                     /db xref="MIM:603876"
                     /translation="MSQTGSHPGRGLAGRWLWGAQPCLLLPIVPLSWLVWLLLLLLAS
                     LLPSARLASPLPREEEIVFPEKLNGSVLPGSGAPARLLCRLQAFGETLLLELEQDSGV
                     QVEGLTVQYLGQAPELLGGAE PGTYLTGTINGDPESVASLHWDGGALLGVLQYRGAEL
                     HLQPLEGGTPNSAGGPGAHILRRKSPASGQGPMCNVKAPLGSPSPRPRRAKRFASLSR
                     FVETLVVADDKMAAFHGAGLKRYLLTVMAAAAKAFKHPSIRNPVSLVVTRLVILGSGE
                     EGPQVGPSAAQTLRSFCAWQRGLNTPEDSDPDHFDTAILFTRQDLCGVSTCDTLGMAD
                     VGTVCDPARSCAIVEDDGLQSAFTAAHELGHVFNMLHDNSKPCISLNGPLSTSRHVMA
                     PVMAHVDPEEPWSPCSARFITDFLDNGYGHCLLDKPEAPLHLPVTFPGKDYDADRQCQ
                     LTFGPDSRHCPQLPPPCAALWCSGHLNGHAMCQTKHSPWADGTPCGPAQACMGGRCLH
                     MDQLQDFNI PQAGGWGPWGPWGDCSRTCGGGVQFSSRDCTRPVPRNGGKYCEGRRTRF
                     RSCNTEDCPTGSALTFREEQCAAYNHRTDLFKSFPGPMDWVPRYTGVAPQDQCKLTCQ
                     ARALGYYYVLEPRVVDGTPCSPDSSSVCVQGRCIHAGCDRIIGSKKKFDKCMVCGGDG
                     SGCSKQSGSFRKFRYGYNNVVTIPAGATHILVRQQGNPGHRSIYLALKLPDGSYALNG
                     EYTLMPSPTDVVLPGAVSLRYSGATAASETLSGHGPLAQPLTLQVLVAGNPQDTRLRY
                     SFFVPRPTPSTPRPTPODWLHRRAOILEILRRRPWAGRK"
                     428..580
    sig peptide
                     /gene≃"ADAMTS4"
                     581..2938
    mat peptide
                     /gene="ADAMTS4"
```

```
/product="a disintegrin and metalloproteinase with
                     thrombospondin motifs-4"
                     665..2833
     misc feature
                     /gene="ADAMTS4"
                     /note="KOG3538; Region: Disintegrin metalloproteinases
                     with thrombospondin repeats [Posttranslational
                     modification, protein turnover, chaperones]"
                     /db xref="CDD:21321"
     misc feature
                     1079..1711
                     /gene="ADAMTS4"
                     /note="Reprolysin; Region: Reprolysin (M12B) family zinc
                     metalloprotease"
                     /db xref="CDD:23198"
                     1739..1954
     misc feature
                     /gene="ADAMTS4"
                     /note="ACR; Region: ADAM Cysteine-Rich Domain"
                     /db xref="CDD:24307"
                     2018..2152
     misc feature
                     /gene="ADAMTS4"
                     /note="TSP1; Region: Thrombospondin type 1 repeats"
                     /db xref="CDD:14922"
     misc feature
                     2486..2833
                     /gene="ADAMTS4"
                     /note="ADAM_spacer1; Region: ADAM-TS Spacer 1"
                     /db xref="CDD:26460"
                     complement (3229)
     variation
                     /allele="G"
                     /allele="C"
                     /db xref="dbSNP:4656992"
                     4308..4313
     polyA signal
                     /gene="ADAMTS4"
                     4331
    polyA site
                     /gene="ADAMTS4"
ORIGIN
        1 gggagaaccc acagggagac ccacagacac atatgcacga gagagacaga ggaggaaaga
      61 qacaqaqaca aaqqcacaqc qqaaqaaqqc aqaqacaqqq caqqcacaqa aqcqqcccag
      121 acagagteet acagagggag aggecagaga agetgeagaa gacacaggea gggagagaca
      181 aagatccagg aaaggagggc tcaggaggag agtttggaga agccagaccc ctgggcacct
      241 ctcccaagcc caaggactaa gttttctcca tttcctttaa cggtcctcag cccttctgaa
      301 aactttgcct ctgaccttgg caggagtcca agcccccagg ctacagagag gagctttcca
      361 aagctagggt gtggaggact tggtgcccta gacggcctca gtccctccca gctgcagtac
      421 caqtqccatq tcccagacag gctcgcatcc cgggaggggc ttggcagggc gctggctgtg
      481 gggageccaa ecetgeetee tgeteeceat tgtgeegete teetggetgg tgtggetget
      541 totgotactg otggoototo tootgoooto agoooggotg gooagoooco toocooggga
      601 ggaggagate gtgtttecag agaageteaa eggeagegte etgeetgget egggegeeee
      661 tgccaggctg ttgtgccgct tgcaggcctt tggggagacg ctgctactag agctggagca
      721 ggactccggt gtgcaggtcg aggggctgac agtgcagtac ctgggccagg cgcctgagct
      781 gctgggtgga gcagagcctg gcacctacct gactggcacc atcaatggag atccggagtc
     841 ggtggcatct ctgcactggg atgggggagc cctgttaggc gtgttacaat atcggggggc
     901 tgaactccac ctccagcccc tggagggagg cacccctaac tctgctgggg gacctggggc
     961 tcacatccta cqccqqaaqa qtcctqccaq cggtcaaggt cccatgtgca acgtcaaggc
     1021 teetettgga ageeceagee eeagaeeeeg aagageeaag egetttgett eactgagtag
     1081 atttgtggag acactggtgg tggcagatga caagatggcc gcattccacg gtgcggggct
     1141 aaagggctac ctgctaacag tgatggcagc agcagccaag gccttcaagc acccaagcat
     1201 ccgcaatcct gtcagcttgg tggtgactcg gctagtgatc ctggggtcag gcgaggaggg
     1261 gccccaagtg gggcccagtg ctgcccagac cctgcgcagc ttctgtgcct ggcagcgggg
     1321 cctcaacacc cctgaggact cggaccctga ccactttgac acagccattc tgtttacccg
     1381 tcaggacctg tgtggagtct ccacttgcga cacgctgggt atggctgatg tgggcaccgt
     1441 ctgtgacccg gctcggagct gtgccattgt ggaggatgat gggctccagt cagccttcac
     1501 tgctgctcat gaactgggtc atgtcttcaa catgctccat gacaactcca agccatgcat
```

11

```
1561 cagtttgaat gggcctttga gcacctctcg ccatgtcatg gcccctgtga tggctcatgt
1621 ggatcctgag gagccctggt ccccctgcag tgcccgcttc atcactgact tcctggacaa
1681 tggctatggg cactgtctct tagacaaacc agaggctcca ttgcatctgc ctgtgacttt
1741 ccctggcaag gactatgatg ctgaccgcca gtgccagctg accttcgggc ccgactcacg
1801 ccattgtcca cagetgccgc cgccctgtgc tgccctctgg tgctctggcc acctcaatgg
1861 ccatgccatg tgccagacca aacactcgcc ctgggccgat ggcacaccct gcgggcccgc
1921 acaggcctgc atgggtggtc gctgcctcca catggaccag ctccaggact tcaatattcc
1981 acaggctggt ggctggggtc cttggggacc atggggtgac tgctctcgga cctgtggggg
2041 tggtgtccag ttctcctccc gagactgcac gaggcctgtc ccccggaatg gtggcaagta
2101 ctgtgagggc cgccgtaccc gcttccgctc ctgcaacact gaggactgcc caactggctc
2221 gagettecca gggeecatgg actgggttee tegetacaea ggegtggeec eecaggaeca
2281 gtgcaaactc acctgccagg cccgggcact gggctactac tatgtgctgg agccacgggt
2341 ggtagatggg accecetgtt ccccggacag etceteggte tgtgtecagg gccgatgcat
2401 ccatgctggc tgtgatcgca tcattggctc caagaagaag tttgacaagt gcatggtqtq
2461 cggaggggac ggttctggtt gcagcaagca gtcaggctcc ttcaggaaat tcaggtacgg
2521 atacaacaat gtggtcacta tccccgcggg ggccacccac attcttgtcc ggcagcaggg
2581 aaaccctggc caccggagca tctacttggc cctgaagctg ccagatggct cctatgccct
2641 caatggtgaa tacacgctga tgccctcccc cacagatgtg gtactgcctg gggcagtcag
2701 cttgcgctac agcggggcca ctgcagcctc agagacactg tcaggccatg ggccactggc
2761 ccagcetttq acactqcaaq tectaqtqqc tqqcaacccc caggacacac gcctccgata
2821 cagettette gtgeecegge egaceette aacgeeaege eccaeteece aggactgget
2881 gcaccgaaga gcacagattc tggagatcct tcggcggcgc ccctgggcgg gcaggaaata
2941 acctcactat cocqqctqcc ctttctqqqc accggqqcct cggacttagc tgggagaaag
3001 agagagette tqttqctqcc tcatqctaaq actcagtggg gaggggctgt gggcgtgaga
3061 cctqccctc ctctctqccc taatgcqcag gctggccctg ccctggtttc ctgccctggg
3121 aggcagtgat gggttagtgg atggaagggg ctgacagaca gccctccatc taaactgccc
3181 cctctqccct qcqqqtcaca ggagggaggg ggaaggcagg gagggcctgg gccccagttg
3241 tatttattta qtatttattc acttttattt aqcaccaggg aaggggacaa ggactagggt
3301 cctggggaac ctgaccctg acccctcata gccctcaccc tggggctagg aaatccaggg
3361 tqqtqqtqat aqqtataaqt qqtqtqtqta tqcqtqtqtg tqtqtqtaa aatqtqtqtq
3421 tgcttatgta tgaggtacaa cctgttctgc tttcctcttc ctgaatttta ttttttggga
3481 aaagaaaagt caagggtagg gtgggccttc agggagtgag ggattatctt tttttttt
3541 totttottto tttottttt ttttttgaga cagaatotog ctctgtcgcc caggotggag
3601 tqcaatqqca caatctcgqc tcactgcatc ctccgcctcc cgggttcaag tgattctcat
3661 gcctcagcct cctgagtagc tgggattaca ggctcctgcc accacgcccg gctaattttt
3721 qttttqtttt qtttqqaqac agaqtctcgc tattqtcacc agggctggaa tgatttcagc
3781 tcactgcaac cttcgccacc tgggttccag caattctcct gcctcagcct cccgagtagc
3841 tgagattata ggcacctacc accacgcccg gctaattttt gtatttttag tagagacggg
3901 gtttcaccat gttggccagg ctggtctcga actcctgacc ttaggtgatc cactcgcctt
3961 catctcccaa aqtqctggga ttacaggcgt gagccaccgt gcctggccac gcccaactaa
4021 tttttqtatt tttaqtaqaq acaqqqtttc accatqttqq ccagqctqct cttqaactcc
4081 tgacctcagg taatcgacct gcctcggcct cccaaagtgc tgggattaca ggtgtgagcc
4141 accacgcccg gtacatattt tttaaattga attctactat ttatgtgatc cttttggagt
4201 cagacagatg tggttgcatc ctaactccat gtctctgagc attagatttc tcatttgcca
4261 ataataatac ctcccttaga agtttgttgt gaggattaaa taatgtaaat aaagaactag
4321 cataacactc aaaaaaaaaa aa
```

<u>Disclaimer</u> | Write to the Help Desk NCBI | NLM | NIH

Feb 24 2004 16:01:25